Cellular reprogramming using vectors based on Sendai virus

Marc Masanas Jimenez, Universitat Autònoma de Barcelona. Biotechnology Degree

Universitat Autònoma de Barcelona

Introduction

Induced pluripotent stem cells (iPSCs) are an attractive tool for disease modelling and future therapeutic applications due to their unlimited proliferative capacity and the minimization of transplant rejections in patients.

There are a wide range of methodologies to obtain iPSCs using cellular reprogramming factors. These methods can be integrative or non-integrative. The main problem of the integrative systems is the integration of the reprogramming factors genes into the cell genome. On the other hand, the major drawback of using non-integrative systems is the low efficiency of the process.

Cellular reprogramming using vectors based on Sendai virus, which codifies for the reprogramming factors, is a non-integrative pathway to obtain iPSCs.

Objectives

- Find out if the utilization of Sendai virus is an efficient non-integrating method to produce iPSCs.
- Discuss if Sendai virus vectors could be employed to produce iPSCs, which are going to be used in regenerative medicine, in the future.

Materials and Methods

- Scientific literature research on PubMed database: current papers and reviews of Sendai virus were selected according to their data of publications and quality.
- Specialized books and reviews about Sendai virus and iPSCs.

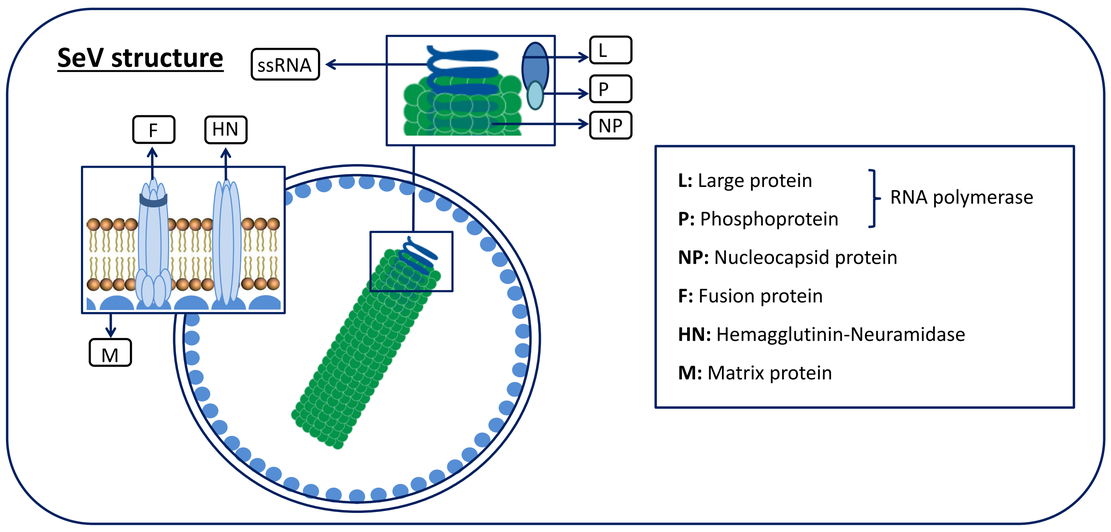
Sendai virus

Sendai virus (SeV) is a pleomorphic enveloped particle with a helical structure. Some promising features of SeV are as follows:

⇨ No human diseases related with SeV have been reported.

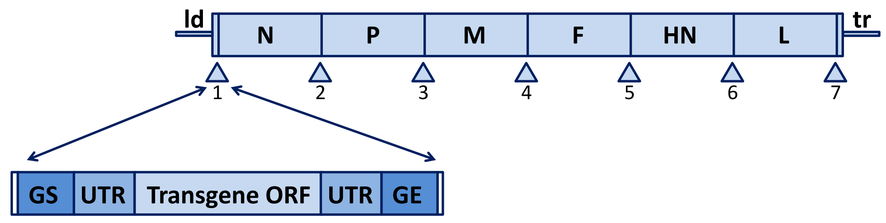
⇨ SeV virus fulfils its lifecycle entirely in the cytoplasm of the infected cells without having a nuclear phase. Therefore, there is no danger of integration into the host genome.

↳ **Could SeV be a good vector to produce iPSCs without risk of tumorigenesis?** Some experimental approaches with different SeV vectors have been performed to investigate this hypothesis.

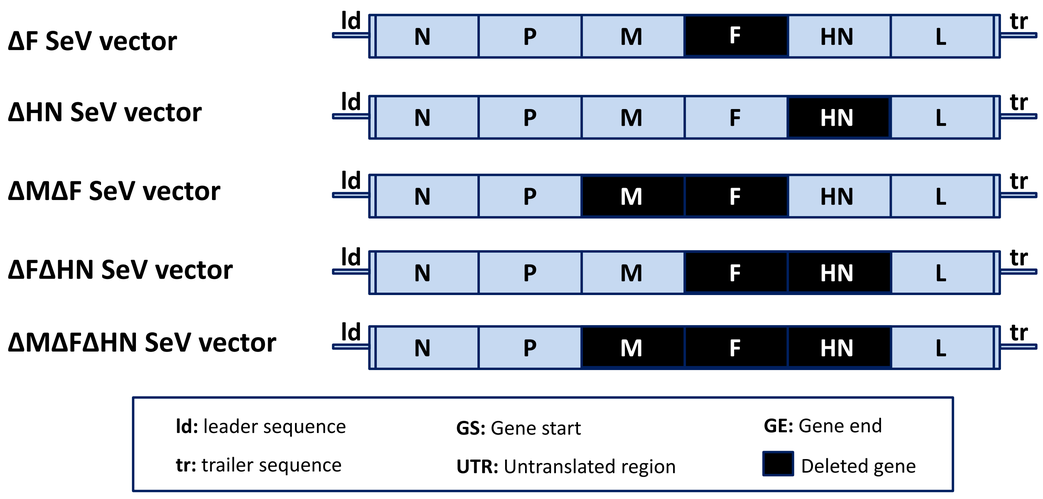


Sendai virus vectors

First-generation SeV vector: SeV *wt* genome carrying the reprogramming factors cDNA.



Second-generation SeV vectors: Some different SeV vectors were designed to avoid the dissemination of SeV vectors to the neighboring cells. To produce replication defective SeV vectors some viral essential genes were deleted.

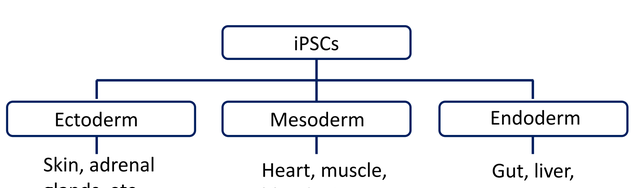


Results

✓ The employment of SeV vectors enabled the efficient generation iPSCs.

✓ Reprogramming factors genes were not integrated into the genome of the target cells. For that reason, no risk of tumorigenesis has been related with this reprogramming method.

✓ Using these vectors, iPSCs which have ability to rise to any cell type of the three germ layers were produced. This fact verifies the pluripotency of the obtained iPSCs.

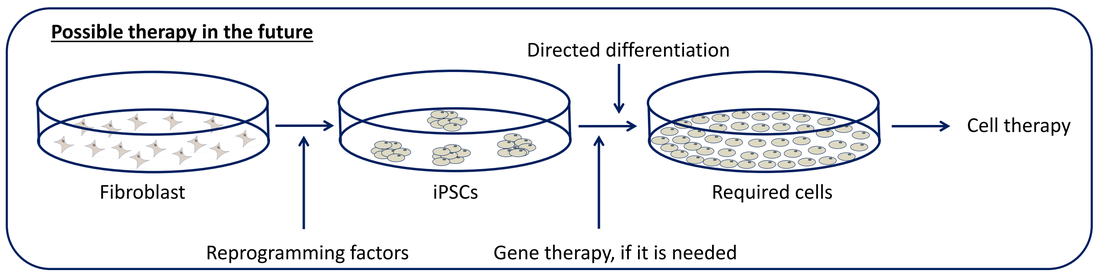


Applications of induced pluripotent stem cells

1. iPSCs area is a promising candidate for **research**. The generation of patient iPSCs enables:

- The study of pathogenic disease mechanism.
- Preclinical drug screening.

2. iPSCs are also attractive for **therapeutic approaches** such as cell therapy.



Conclusions

- The generation of iPSCs using SeV vectors is promising due to its efficiency.
- There is no guarantee that the utilization of SeV vectors to produce iPSCs will be used in the future in regenerative medicine. The utilization of high temperatures to remove viral genomes may produce mutations or rearrangements in iPSCs; for that reason, more investigation is needed to check that cells do not mutate in these conditions.

Further information

Malik, N. and Rao, M. (2013) A review of the mothods for human iPSC derivation. *Methods Mol. Biol.*, **997**, 23-33.

Nakanishi, M. and Otsu, M. (2012) Development of Sendai Virus Vectors and their Potential Applications in Gene Therapy and Regenerative Medicine. *Curr. Gene Ther.*, **12**, 410-416.